AMENDMENTS TO THE SPECIFICATION

On page 1, line 3, please delete -- is related to provisional patent applications --,
and insert --- claims the benefit of U.S. Provisional Applications Nos . ---.

This amendment clarifies that a benefit claim is being made to provisional applications 60/315,394 and 60/324,155.

A specification replacement sheet is attached indicating the changes made.

Applicants have attached, to this amendment, a petition to accept a delayed claim benefit for the indicated application.

If there are any questions or concerns, please contact the undersigned.

Respectfully submitted,

Mark K. Johnson Reg. No. 35,909
Mirus
505 South Rosa Road
Madison, WI 53719
608-238-4400

I hereby certify that this correspondence is being sent by facsimile transmission to: Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450 on this date: 8/19/2004.

Kirk Ekena

[REPLACEMENT SHEET]

Inhibition Of Gene Expression By Delivery Of Small Interfering RNA To Post-Embryonic Animal Cells *In vivo*

This Patent Application ~~is related to provisional patent applications~~ claims the benefit of U.S. Provisional Applications Nos. 60/315,394 filed August 27, 2001 and 60/324,155 filed September 20, 2001; and is a Continuation-In-Part of United States Patent Applications serial numbers 09/707,117 filed November 6, 2000 and 09/877,436 filed on June 7, 2001, which is a divisional of 09/450,315 filed Nov. 29, 1999, now Pat. No. 6,379,966, which claims priority of provisional applications 60/121,730 filed on Feb. 26, 1999 and 60/146,564 filed on Jul. 30, 1999.

FIELD

The present invention generally relates to inhibiting gene expression. Specifically, it relates to inhibiting gene expression by delivery of small interfering RNAs (siRNAs) to post-embryonic animals.

BACKGROUND

RNA interference (RNAi) describes the phenomenon whereby the presence of double-stranded RNA (dsRNA) of sequence that is identical or highly similar to a target gene results in the degradation of messenger RNA (mRNA) transcribed from that targeted gene (Sharp 2001). RNAi is likely mediated by siRNAs of approximately 21-25 nucleotides in length which are generated from the input dsRNAs (Hammond, Bernstein et al. 2000; Parrish, Fleenor et al. 2000; Yang, Lu et al. 2000; Zamore, Tuschl et al. 2000; Bernstein, Caudy et al. 2001).

The ability to specifically knock-down expression of a target gene by RNAi has obvious benefits. For example, RNAi could be used to generate animals that mimic true genetic "knockout" animals to study gene function. In addition, many diseases arise from the abnormal expression of a particular gene or group of genes. RNAi could be used to inhibit the expression of the genes and therefore alleviate symptoms of or cure the disease. For example, genes contributing to a cancerous state could be inhibited. In addition, viral genes could be inhibited, as well as mutant genes causing dominant genetic diseases such as myotonic dystrophy. Inhibiting such genes as cyclooxygenase or cytokines could also treat inflammatory diseases such as arthritis. Nervous system disorders could also be treated. Examples of targeted organs would include the liver, pancreas, spleen, skin, brain, prostrate, heart etc.